UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/623,038	11/27/2000	George M. Carlone	65446	5598

23859 7590 07/23/2004

NEEDLE & ROSENBERG, P.C.
SUITE 1000
999 PEACHTREE STREET
ATLANTA, GA 30309-3915

EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 07/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/623,038	CARLONE ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-12,15,16,18 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *72202 (page 2 only)*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendments

1) Acknowledgment is made of Applicants' amendment filed 12/15/03 in response to the non-final Office Action mailed 08/27/03 and Applicants' amendment filed 5/6/04. With this, Applicants have amended the specification.

Status of Claims

2) Claims 1, 6, 12, 15 and 20 have been amended via the amendment filed 12/15/03.

Claims 1-22 are pending.

Claims 1-6, 8-12, 15, 16, 18 and 20, to the extent these claims encompass SEQ ID NO: 6, are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Information Disclosure Statement

5) Applicants request the Office to consider the reference, B9, in the information disclosure statement filed 7/22/02. The reference was considered previously, but the initialing was left out due to an oversight. An initialed page 2 of the IDS is attached to this Office Action for Applicants' record.

Objection(s) Withdrawn

6) The objection to the specification made in paragraph 7 of the Office Action mailed 08/27/03 with regard to the sequence non-compliance is withdrawn upon further consideration.

7) The objection to the specification made in paragraph 9(a) of the Office Action mailed 08/27/03 is withdrawn in light of Applicants' amendment to the specification.

8) The objection to the specification made in paragraph 9(b) of the Office Action mailed 08/27/03 is withdrawn in light of Applicants' amendment to the specification.

Objection(s) Maintained

9) The objection to claims 6, 12, 15 and 20 made in paragraph 20 of the Office Action mailed 08/27/03 is maintained for reasons set forth therein.

Rejection(s) Withdrawn

10) The rejection of claims 1, 15 and those dependent therefrom made in paragraph 11 of the Office Action mailed 08/27/03 under 35 U.S.C. § 101 as being directed to non-statutory subject matter, is withdrawn in light of Applicants' amendment to the claims and/or the base claim(s).

11) The rejection of claims 6, 12, 15, 16, 18 and 20 made in paragraph 13 of the Office Action mailed 08/27/03 under 35 U.S.C. § 112, first paragraph, as containing inadequate written description, is withdrawn, in light of Applicants' amendments to the claims.

12) The rejection of claim 6 made in paragraph 14 of the Office Action mailed 08/27/03 under 35 U.S.C § 112, first paragraph, as being non-enabled with regard to the scope of the claims in relation to 'fragments', is withdrawn in light of Applicants' amendment to the claim.

13) The rejection of claims 6, 12, 15 and 20 made in paragraph 15(a) of the Office Action mailed 08/27/03 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claims.

14) The rejection of claims 1, 8, 12 and 20 made in paragraph 15(b) of the Office Action mailed 08/27/03 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claims.

15) The rejection of claim 15 made in paragraph 15(c) of the Office Action mailed 08/27/03 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claim.

16) The rejection of claims 6 and 15 made in paragraph 15(d) of the Office Action mailed 08/27/03 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claims.

17) The rejection of claims 12 and 20 made in paragraph 15(e) of the Office Action mailed 08/27/03 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claims.

18) The rejection of claims 2-5, 9-11, 16 and 18 made in paragraph 15(f) of the Office Action mailed 08/27/03 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claims and/or the base claim(s).

19) The rejection of claims 12, 15, 16, 18 and 20 made in paragraph 13 of the Office Action mailed 08/27/03 under 35 U.S.C. § 112, first paragraph, as containing inadequate written description, is withdrawn.

Rejection(s) Maintained

20) The provisional rejection of claims 1-6, 12, 15, 16, 18 and 20 made in paragraph 16 of the Office

Action mailed 08/27/03 under the judicially created doctrine of obviousness-type double patenting over claims 1, 2, 8 and 12-14 of the co-pending application SN 09/613,092, is maintained for reasons set forth therein.

Applicants ask that because the scope of the instant claims and the claims of the co-pending application 09/613,092 may change during the course of prosecution, a terminal disclaimer be postponed until the time of allowance. The rejection will be maintained until then.

21) The rejection of claim 2 made in paragraph 12 of the Office Action mailed 08/27/03 under 35 U.S.C. § 112, first paragraph, with regard to the deposit issue, is maintained for reasons set forth therein and herebelow.

Applicants cite MPEP 2164 and contend that the enablement requirement is met if one of skill in the art is enabled to make and use that which is defined by the claims. Applicants state that the standard for determining whether the specification meets the requirement is: 'is the experimentation needed to practice the invention undue or unreasonable?' Applicants state that the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. Applicants submit that the *Wands* factors are not limiting and can be used to determine if there is sufficient evidence to support a determination that a disclosure does not satisfy the requirement. Applicants assert that before any analysis of enablement can occur, the claims must be construed, and that the Office has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. Applicants submit that claim 2 is not directed to the listed monoclonal antibodies themselves, instead, to a peptide that immunospecifically binds to the listed monoclonal antibodies. Applicants state that the hybridomas and their respective monoclonal antibodies are disclosed in US patent 5,854,416 as indicated in the instant specification on page 12, which patent has been incorporated into the present application by incorporation. Applicants contend that antibodies can be prepared by many well known methods as indicated in pages 19 and 23, and Examples 1, 8 and 12 of the specification.

Applicants' arguments have been carefully considered, but are non-persuasive. Applicants are correct in that claim 2 is not drawn to a monoclonal antibody. However, in order to make the claimed peptide that is required to immunospecifically bind to the specific monoclonal antibody recited in claim 2, one has to have public access to the same monoclonal antibody. Despite the fact that methods of producing monoclonal antibodies are well known in the art, it would require undue experimentation for one of skill in the art to produce the exact same monoclonal antibody recited in the claim having the exact same binding characteristics or immunospecificity. Exact replication of the cell lines producing the recited monoclonal antibodies is an unpredictable event. Although respective monoclonal antibodies are disclosed in US patent

5,854,416, from the '416 patent it does not appear that hybridoma cell lines producing these monoclonal antibodies are publicly available except for the group to whom the '416 patent has been issued. There is no evidence of record that the hybridoma cell lines secreting the recited monoclonal antibodies may be reproducibly produced without undue experimentation, or that a suitable deposit has been made for patent purpose. A mere recitation of the various specific monoclonal antibodies is insufficient to meet the conditions under 37 C.F.R 1.801-1.809.

22) The rejection of claims 12, 15, 16, 18 and 20 made in paragraph 14 of the Office Action mailed 08/27/03 under 35 U.S.C § 112, first paragraph, as being non-enabled with regard to the scope, is maintained for reasons set forth therein and herebelow.

With regard to the peptide variants having 80% identity to SEQ ID NO: 6 or an immunogenic fragment of 80% identical peptide variants of SEQ ID NO: 6, Applicants contend that page 19 discusses using procedures to identify and produce an allelic immunogenic peptide. Applicants state that lines 9-20 on page 22 and Examples 4-7 and 14 discuss how to identify immunogenic fragments that elicit protective immunity and how to screen the identified peptides. Applicants submit that 'even if significant experimentation may be necessary, there is sufficient guidance within the specification to make the experimentation necessary to make and use the claimed peptides and compositions simply routine'.

Applicants' arguments have been carefully considered, but are non-persuasive. The peptide, the peptide variant with 80% identity, and/or immunogenic fragments thereof claimed in claims 12, 16, 18 and 20 are required to confer protective immunity against *S. pneumoniae* infection. The peptide variant or an immunogenic fragment thereof claimed in claim 15 is required to be at least *S. pneumoniae*-specific. As set forth previously, unpredictability is one of *Wands* factors for enablement. In the instant case, the claimed peptide variant having at least 80% sequence identity to the peptide of SEQ ID NO: 6 is required to be immunogenic, diagnostic and/or are protective against *S. pneumoniae* such that it is of use as a therapeutic, prophylactic or diagnostic composition. The claimed peptide variant is minimally required to be *S. pneumoniae*-specific. Although a microbial polypeptide or protein is expected in the art to generally induce specific antibodies, the ability of peptide variants having at least 80% sequence identity, i.e., as much as 20% non-identity, to the peptide of SEQ ID NO: 6, to confer protective immunity against a microbial disease, pneumonia in the instant case, or to serve as a *S. pneumoniae*-specific diagnostic reagent, is not predictable. The instant specification fails to teach how to produce a peptide variant having at least 80% sequence identity to the peptide of SEQ ID NO: 6 such that it is capable of serving as a specific diagnostic or therapeutic/prophylactic composition and is capable of conferring protective immunity to *S. pneumoniae* infection in a human or non-human subject, or capable of diagnosing *S. pneumoniae* infections. The

specification provides no guidance as to which specific amino acids must be retained and which may be varied within the peptide of SEQ ID NO: 6 without causing any detrimental effect to the claimed peptide that is meant to induce a protective immune response in a subject against *S. pneumoniae* infection or to diagnose a *S. pneumoniae* infection. There is no guidance in the instant specification with regard to which amino acid variations, i.e., insertions, deletions, additions and substitutions, in the peptide would result in a peptide variant of the recited percent identity or an immunogenic fragment thereof that would retain the three-dimensional structure and the functional integrity or biological/immunogenic competence of the native protein or peptide, without rendering it non-functional. Except for a full length 37-kDa protein of *S. pneumoniae* that confers protective immunity against challenge with a wild-type *S. pneumniae,* there appears to be no evidence within the instant specification, as originally filed, showing that the peptide of SEQ ID NO: 6, or an immunogenic fragment thereof, or a variant thereof having 80% sequence identity to the peptide of SEQ ID NO: 6 is capable of conferring protective immunity against *S. pneumoniae* or capable of detecting *S. pneumoniae* in a diagnostic assay. There appears to be not even a showing that the unmodified 15 amino acid-long peptide of SEQ ID NO: 6, let alone its immunogenic fragment or variant having at least 80% sequence identity, does indeed confer protective immunity against *S. pneumoniae* or detects *S. pneumoniae* infection via a diagnostic assay. A review of the specification suggests that the 'Results' section on page 31 and Example 4 of the specification describe the protective ability of the full length 37-kDa protein of *S. pneumoniae*. Table 4 shows that the peptide of SEQ ID NO: 6 is 1B6 mAb-specific. Example 14 shows that the peptide of SEQ ID NO: 6, when conjugated to KLH and mixed with an adjuvant, is immunogenic in mice. The protection experiments described in Examples 4 and 5 are limited to a showing that the whole 37-kDa protein of *S. pneumoniae* confers protection in mice against challenge with a wild-type *S. pneumoniae*. The specific monoclonal antibodies recited in the claims were generated using the 37-kDa protein, and not by using the claimed peptide. There is no showing that the peptide of SEQ ID NO: 6, an immunogenic fragment thereof, or a variant thereof having at least 20% dissimilarity to SEQ ID NO: 6, is protective against *S. pneumoniae*. The *S. pneumoniae*-specificity of an immunogenic fragment of the peptide of SEQ ID NO: 6, or a variant of the peptide of SEQ ID NO: 6, or an immunogenic fragment of the variant as recited, is not established. This is important because the art reflects unpredictability as to which amino acids in a specific protein can be varied, i.e., replaced or added, without adversely affecting the functional properties of that specific protein. While it is known in the art that variation in one or more amino acids is possible in a given protein, the exact position within its amino acid sequence where replacements or variations can be made, with a reasonable expectation of success of retaining the protein's functional integrity, is not certain. A random replacement affecting the epitopic amino acid positions that are critical, for example, to the three-

dimensional conformational structure and specific binding property of the protein, would result in a polypeptide that may be non-functional (i.e., non-immunogenic) or not optimally immunogenic or protective as a vaccine candidate, because such positions tolerate no or little modifications. As set forth previously, Houghten *et al.* (New Approaches to Immunization, *Vaccines86*, Cold Spring Harbor Laboratory, p. 21-25, 1986) teach the criticality of individual amino acid residues and their positions in peptide antigen-antibody interactions. Houghten *et al.* state (see page 24):

> One could expect point mutations in the protein antigen to cause varying degrees of loss of protection, depending on the relative importance of the binding interaction of the altered residue. A protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies in the polyclonal pool.

Thus, the art reflects that variations in critical residues at specific positions in an amino acid sequence could result in a polypeptide which may induce an antibody that may not recognize or bind to the native polypeptide of a microorganism. In the instant case, this is important because one of the purposes of the instant invention is to produce a peptide variant of *S. pneumoniae* or an immunogenic fragment thereof in its biologically active, immunogenic and/or protective form for inducing a protective immune response or diagnosing a *S. pneumoniae* infection. The instant disclosure lacks guidance on the precise position(s), nature and extent of amino acid replacements or variations that can be made in the claimed peptide in order to produce a variant with 80% identity to SEQ ID NO: 6 or an immunogenic 'fragment' thereof or, and with regard to whether it would serve as an effective immunogen capable of conferring protective immunity against *S. pneumoniae* infection in a human or a non-human subject, or as an effective *S. pneumoniae*-specific diagnostic reagent.

Therefore, undue experimentation would have been required to reproducibly practice the full scope of the invention as claimed currently, due to the lack of adequate and specific guidance, the lack of evidentiary support in the specification enabling a protective peptide of SEQ ID NO: 6, a protective or *S. pneumoniae*-specific variant peptide having at least 80% sequence identity to SEQ ID NO: 6 or an immunogenic fragment thereof, the nature of the invention, the state of the prior art, the quantity of experimentation necessary, and the art-demonstrated unpredictability in determining amino acid variations that are acceptable. *Ex parte Foreman, 230 USPQ 546, 547 (Bd. Pat. Appls. And Interf. 1986)*. One of skill in the art would not have been able to make the claimed product and use it, for example, for inducing anti-pneumococcal protective immune response in a subject, or as an *S. pneumoniae*-specific diagnostic reagent, without undue experimentation, because there is no disclosure as to what positions and what specific amino acid residues are varied or truncated. The claims are viewed as not meeting the scope of enablement

provisions of 35 U.S.C § 112, first paragraph. The rejection stands.

23) The provisional rejection of claims 1-5 and 8-11 made in paragraph 18 of the Office Action mailed 08/27/03 under 35 U.S.C § 102(e) as being anticipated by Sampson *et al.* (US 6,217,884), is maintained for reasons set forth therein and herebelow.

Applicants allege that the claims have been misread and misconstrued. Applicants submit that what is claimed is not a monoclonal antibody, the PsaA itself, or fragments of PsaA , but a composition comprising a purified peptide that immunospecifically binds to a monoclonal antibody obtained in response to immunizing an animal with PsaA. Applicants assert that the claimed peptide binds to the monoclonal antibody. Applicants acknowledge that Sampson *et al.* ('884) disclose an isolated nucleic acid of SEQ ID NO: 1 which encodes the 37 kDa PsaA of SEQ ID NO: 2 and a polypeptide encoded by the nucleic acid comprising a unique fragment of at least 10 nucleotides of SEQ ID NO: 1. Applicants acknowledge that columns 11-12 of Sampson *et al.* ('884) disclose fragments of the 37 kDa PsaA and that columns 12-13 disclose polyclonal and monoclonal antibodies which bind to the polypeptide encoded by a unique fragment of at least 10 nucleotides of SEQ ID NO: 1. Applicants agree that Sampson *et al.* ('884) disclose that an antibody can be raised to the PsaA fragment. Applicants readily admit that at lines 16-46 at column 13, Sampson *et al.* ('884) disclose a vaccine comprising an immunogenic polypeptide encoded by a unique fragment of at least 10 nucleotides of SEQ ID NO: 1. Applicants allege that column 10 in the '884 patent has been misread. Applicants state that lines 16-67 of column 10 of the '884 patent describe a method of producing a 37 kDa pneumococcal surface adhesin protein by linking two peptides or polypeptides together by protein chemistry techniques. Applicants argue that these shorter and larger peptides and partial polypeptides 'may' or may not be immunogenic and that shorter sequences are joined to form the 37 kDa protein itself.

Applicants' arguments have been carefully considered, but are non-persuasive. As Applicants acknowledge, Sampson *et al.* ('884) disclosed PsaA fragments, i.e., peptides, encoded by a unique at least 10 nucleotides of SEQ ID NO: 1, and larger peptides. The phrase 'at least 10 nucleotides of SEQ ID NO: 1' encompasses 20 nucleotides, 30 nucleotides, 40 nucleotides, 50 nucleotides, 60 nucleotides etc. As Applicants acknowledge, Sampson's monoclonal and polyclonal antibodies bind to such a polypeptide fragment or peptide. One of skill in the art would expect at least larger peptides or partial polypeptides from the 37 kDa protein to be immunogenic. One of skill in the art would reasonably expect at least one of Sampson's PsaA fragments to bind immunospecifically to at least one of the monoclonal antibodies recited in claim 1. Thus, claims have not been misread and misconstrued. The disclosure of Sampson *et al.* ('884) anticipates the instant claims.

24) The rejection of claims 1, 6 and 15 made in paragraph 19 of the Office Action mailed 08/27/03 under 35 U.S.C § 102(b) as being anticipated by Nuijens *et al.* (WO 9117258) as evidenced by Harlow *et al.* (*In*: *Antibodies*: *A Laboratory Manual*. Cold Spring Harbor Laboratory, Chapter 5, p. 76, 1988), is maintained for reasons set forth therein and herebelow.

Applicants acknowledge that Nuijens's Example II discloses a peptide with the amino acid sequence N-phe-ser-pro-val-**ser-tyr-gln-his-asp-leu**-ala-leu-C, which is a 12 amino acid peptide. Applicants assert that SEQ ID NO: 6 of the present invention is a 15 amino acid peptide: Arg-Ser-Tyr-Gln-His-Asp-Leu-Arg-Ala-Tyr-Gly-Phe-Trp-Arg-Leu. Applicants submit that although a portion of the sequences overlap, Nuijens's sequence does not anticipate the sequence of SEQ ID NO: 6. Applicants state that the fragment is an 'immunogenic fragment' and that the peptide of claim 15 is at least 80% identical to SEQ ID NO: 6, or at least 80% identical to an immunogenic fragment of SEQ ID NO: 6. Applicants allege that the attached sequence alignment shows a 40% query match of SEQ ID NO: 6. Applicants argue that Nuijens *et al.* do not disclose whether the 6 amino acid overlapping section of the peptide is immunogenic or immunogenic against *S. pneumoniae*. Applicants allege that the Office has not demonstrated whether the 6 amino acid sequence falls within the claims of the present invention.

Applicants' arguments have been carefully considered, but are non-persuasive. Contrary to Applicants' assertion, Nuijens' peptide is not a large sequence and it does not represent the entire human genome or the entire protein. Claim 1 does not place any size limit on the claimed peptide. Claim 1 fails to identify the claimed peptide by its structure, i.e., SEQ ID number. Therefore, the claimed peptide does not exclude Nuijens's SYQHDL-containing peptide. Since the recited peptide or protein is not identified by one or more structural limitations, it encompasses Nuijens's synthetic peptide. The instant claims contain a functional limitation without reciting any structure. Via the sequence identity with a six amino acid-long peptide from the SEQ ID NO: 6 of the instant specification, the Office has established that the prior art peptide has the exact identical structure of a peptide or fragment from SEQ ID NO: 6, SYQHDL, which is long enough to serve as an antigenic determinant or epitope. The source of this structurally identical peptide is irrelevant since a chemically synthesized peptide, not isolated *per se* from *Streptococcus pneumoniae,* is also encompassed within the scope of the claim. Thus, Applicants' argument that there is no basis for similarity of structure or functional or immunogenic correlation is inaccurate. The functional limitation, on which the prior art reference is silent, is considered as an intrinsic property of the prior art peptide, or a function of the prior art peptide uncharacterized at that time. With regard to Applicants' remark on the immunogenic nature of the peptide, it should be noted that SYQHDL does form an epitope for the PsaA-specific monoclonal antibody, 1B6, as evidenced by the teachings of Srivastava *et al.* (*Hybridoma* 19: 23-31,

2000). The SYQHDL epitope-containing peptide existed at the time of the invention as taught by Nuijens *et al.* at line 13 on page 14 under Example II. Where the only difference between the claimed product and the prior art product is recited in the functional language, i.e., by what it does rather than what it is, it is incumbent upon Applicants, when challenged by the USPTO, to demonstrate that the prior art product does not actually possess those characteristics. Applicants have not shown that the underlying structure of the prior art peptide, SYQHDL, differs from that of the instantly recited peptide. The mere functional limitation does not impart a specific structure that distinguishes the peptide of the prior art from the recited peptide. It should be noted that Nuijens *et al.* taught using the SYQHDL-containing peptide as an immunogen by conjugating to a protein carrier. Furthermore, Nuijens' SYQHDL qualifies as an immunogenic fragment of Applicants' SEQ ID NO: 6. The rejection stands.

Remarks

25) Claims 1-6, 8-12, 15, 16, 18 and 20 stand rejected.

For clarity, in claims 3, 4 and 9-12, it is suggested that Applicants replace the recitation 'residues in length' with the recitation --amino acid residues in length--.

This application contains claims drawn to non-elected inventions. A complete response to the final rejection must include cancellation of non-elected claims and non-elected subject matter or other appropriate action (37 CFR 1.144). MPEP § 821.01.

26) Applicants' amendments necessitated the new ground(s) of rejection presented in this Office action. **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

27) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is

(703) 872-9307.

28) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

29) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system. A message may be left on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

July, 2004

S. DEVI, PH.D.
PRIMARY EXAMINER